Adaptation of cancer cells from different entities to the MDM2 inhibitor nutlin-3 results in the emergence of p53-mutated multi-drug-resistant cancer cells

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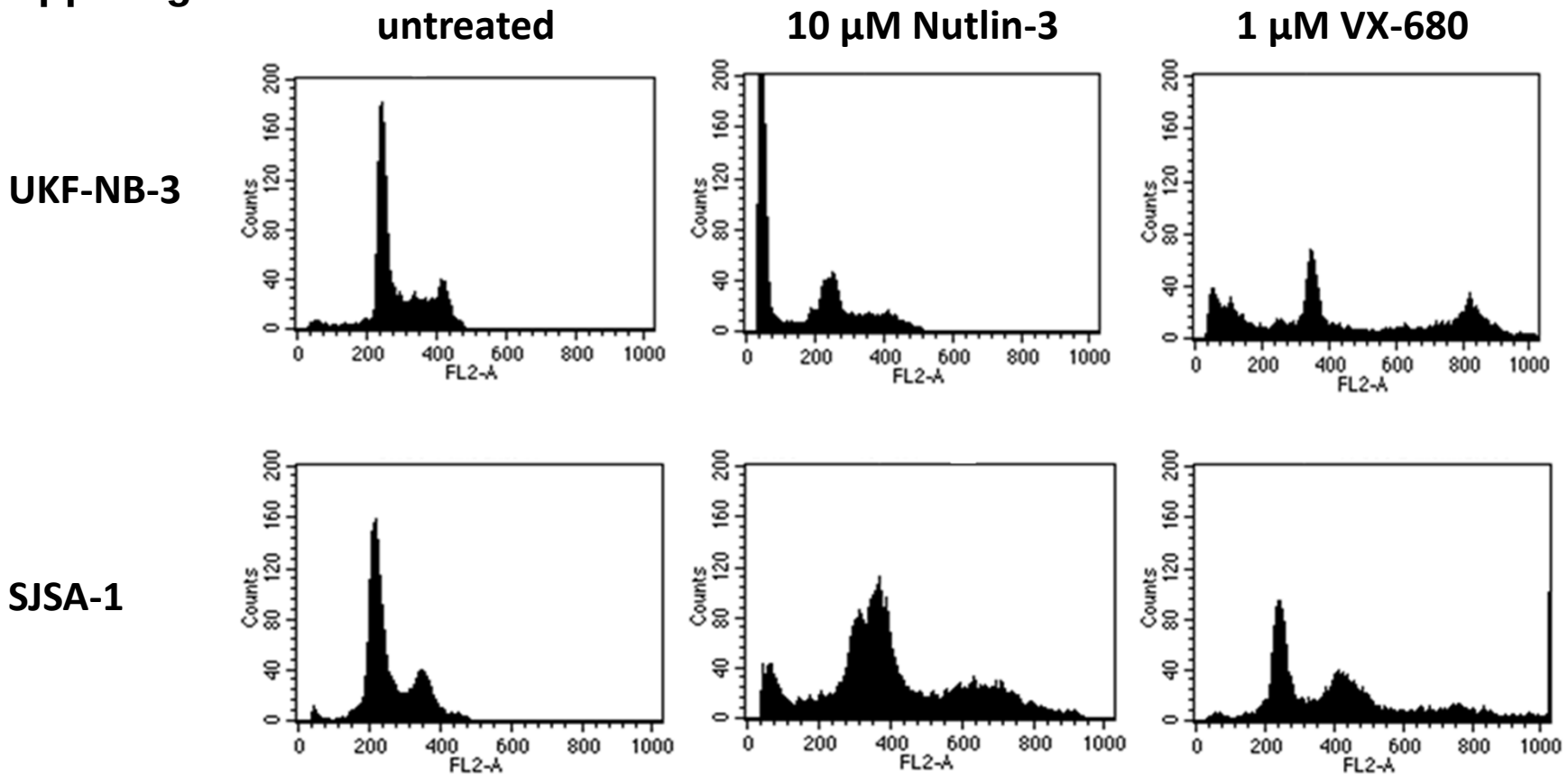
Suppl. Figure 1



Suppl. Figure 1. Detection of DNA content in different cell lines after treatment with nutlin-3 or the aurora kinase inhibitor VX680. Cells were fixed with 70 % ethanol for two hours at -20°C. The cellular DNA was stained using propidi um iodide (20 µg/ml, purchased from Sigma-Aldrich Chemie GmbH, Munich, Germany) and analysed by flow cytometry (FacsCalibur, BD Biosciences, Heidelberg, Germany).

Previous investigations had shown that transient treatment of osteosarcoma cells with nutlin-3 resulted in the formation of tetraploid clones (Shen et al., 2008). Here, nutlin-3 induced tetraploidy in osteosarcoma SJSA-1 cells but not in UKF-NB-3 cells. In contrast, treatment with the aurora kinase inhibitor VX-680 that is known to induce tetraploidy (Harrington et al., 2004) resulted in a fraction of cells with a DNA content ≥ 4N.

References:

Harrington EA, Bebbington D, Moore J, Rasmussen RK, Ajose-Adeogun AO, Nakayama T, Graham JA, Demur C, Hercend T, Diu-Hercend A, Su M, Golec JM, Miller KM. VX-680, a potent and selective small-molecule inhibitor of the Aurora kinases, suppresses tumor growth in vivo. Nat Med 2004;10:262-7.

Shen H, Moran DM, Maki CG. Transient nutlin-3a treatment promotes endoreduplication and the generation of therapy-resistant tetraploid cells. Cancer Res 2008;68:8260-8.